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SPLENECTOMY IN MASSIVE TROPICAL SPLENOMEGALY: TWO- TO SIX-YEAR FOLLOW-UP IN 14 PATIENTS*

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Abstract. Between 1978 and 1982, 14 patients underwent splenectomy for disabling, massive splenomegaly at the Regency Hospital in Wamena in the highlands of Irian Jaya, Indonesia. All patients were clinically diagnosed as having tropical splenomegaly syndrome (hyperreactive malarial splenomegaly), but in no case was the diagnosis confirmed. In May 1984 nurses and physicians caring for these 14 patients were asked to fill in a questionnaire regarding the patients' conditions. Two to 6 years after splenectomy, 8 of the 14 patients were alive and able to work; at least 6 of the 8 at normal or near normal capacity. One patient died 4 days after surgery and 5 died from 2 to 20 months after surgery. We conclude that splenectomy is beneficial for some highly selected patients with the clinical diagnosis of tropical splenomegaly syndrome.

Key words: Splenectomy; splenomegaly; tropical splenomegaly; tropical splenomegaly syndrome; hyperreactive malarial splenomegaly; splenectomy in tropical splenomegaly; Irian Jaya; Indonesia

Introduction

The role of splenectomy in the treatment of tropical splenomegaly syndrome (TSS), also known as hyperreactive malarial splenomegaly (HMS), is not well defined [1]. Since the early 1970's long-term malaria chemoprophylaxis has been considered the treatment of choice [1-5]. However, approximately 20% of patients in New Guinea [5] and in Flores, Indonesia (Hoffman, unpublished) do not respond as expected to chemoprophylaxis, and some individuals with TSS (HMS) are severely incapacitated even after years of chemoprophylaxis. Splenectomy for TSS (HMS) is usually associated with a dramatic improvement in the patients' general condition and hematologic abnormalities [6-8]. While there is considerable concern about late post-operative mortality secondary to overwhelming infection, there have been no complete, prospective, longitudinal follow-up studies which assessed general condition, productivity, and mortality after splenectomy in patients with TSS (HMS). One reason for the lack of such studies is that most patients with TSS (HMS) are cared for in hospitals where facilities for establishing the diagnosis [1,5] of TSS (HMS) are not available. Another reason is that follow-up of patients, many of whom come from remote villages, is often difficult.

* The opinions and assertions contained herein are those of the authors and are not to be construed as official or as reflecting the views of the Indonesian Ministry of Health or the United States Navy.

We report the two- to six-year follow-up of all 14 patients who had elective splenectomy for massive, disabling splenomegaly, thought, but not confirmed, to be tropical splenomegaly syndrome (HMS), at the Regency Hospital in the Baliem Valley of the highlands of Irian Jaya; Indonesia (West New Guinea) from June 1978 through March 1982. In July 1984, 8 of the 14 were alive and working productively.

Methods

Patient population and study site. All patients were autochthonous Irianese and all except one were born and had lived their entire lives on the northern and southern slopes (50-1200 meters above sea level) of the central highlands of Irian Jaya. They were hunters, gatherers, and farmers who lived a subsistence existence in the forest and swamps in small, isolated communities of 50-200 people without electricity, plumbing, or vehicular access to other villages. Most lived several days' walk from the nearest health station. One patient, a teacher, was born in coastal Biak, Indonesia, and had lived for 5 years on the lower slopes. Recent surveys and the experience of physicians in the area indicate that malaria is mesoendemic on the slopes (parasite point prevalence 35-50% in children aged 2-9) and that massive splenomegaly in adults is common (Zaini, unpublished). All operations were performed by one of us (WHV) at the Kabupaten (Regency) hospital at Wamena in the Baliem Valley of the central highlands of Irian Jaya (1500 meters above sea level).

Patient selection and indications for surgery. All patients were referred to the hospital in Wamena by village health workers, nurses, or doctors. Patients had received long-term malaria chemoprophylaxis or repeated malaria therapy without success. The referring health workers chose only the most severely debilitated from among many patients with massive splenomegaly in their areas. The major reason for referral was an inability to live or work normally because of massive splenomegaly, splenic pain, or debilitation. In Wamena the indications for surgery were inability to work because of severe debilitation, splenic pain, or abdominal mass with or without anaemia refractory to treatment. All patients were diagnosed clinically as having tropical splenomegaly syndrome (TSS) (HMS). In no case was the diagnosis confirmed [1, 5].

Pre-operative assessment and management. A history, physical examination, and hemoglobin determination were done at the time of admission. The Hackett spleen grade [9], liver size, presence of ascites, and presence of abdominal varices were specifically noted. Patients were graded as to general condition, weakness, spleen pain, and abdominal mass. Any obvious infections were treated pre-operatively with antimicrobials. No pre-operative blood transfusions were given.

Operative and post-operative management. After appropriate preparation the abdomen was entered by a subcostal, paramedian, or combined paramedian and transverse abdominal incision, depending on the size of the spleen. The spleen was mobilized by cutting its ligaments and the tail of the pancreas identified. If possible the splenic artery and vein were immediately isolated and ligated and the spleen was removed. The appearance of the liver was noted, ascites drained, and the wound closed without drainage. In three cases the spleen was weighed, and in all cases the presence of capsular thickening, adhesions, and infarctions were noted.

Post-operatively, patients were treated with 600,000 units of procaine penicillin and 1 gram of streptomycin intramuscularly once a day for 4-5 days. Patients were discharged when they were ambulatory and their wounds had healed. It was recommended that they be placed on permanent malaria chemoprophylaxis.

Post-operative follow-up. In May 1984, a questionnaire was sent to registered nurses and physicians working in the areas where the patients lived. The nurses and physicians were asked to determine each patient's condition. If the patient was alive, the health worker was asked to examine the patient and record the general condition (normal, weak, very weak), what the patient thought his condition was, compared with preoperatively (much better, better, the same, worse), and what the patient thought his capacity to work was (full-time, 75%, 50%, 25%, not at all). If the patient had died, the worker was asked to record the approximate date of death, the apparent cause of death, and whether it appeared that the patient had malaria or another infection at the time of death.

Results

Patients. From June 1978 through March 1982, 15 patients with a clinical diagnosis of TSS (HMS) were taken to the operating room for elective splenectomy. One of the 15 patients (patient E1) with a Hackett grade 2 spleen was found to have ascites and a severely nodular, cirrhotic liver, and splenectomy was not performed. The other 14 had splenectomies. In July 1984, 8 of the 14 patients were alive. The pre-operative clinical characteristics of the 14 patients are outlined in *table 1*. Ten of the 14 patients had multiple indications for surgery (see Methods). Six patients had ascites and one had abdominal varices (late fatality). No patient had a history of gross gastrointestinal bleeding.

During the observation period (1978-1982) only one other patient (E2) had a splenectomy. The history and the hospital and post-hospital course of this patient and the patient noted above who did not have a splenectomy are described below.

Operative findings and post-operative hospital course. The operative findings in the eight patients who are still alive, the five patients who died from 2 to 20 months after surgery (late fatality), and the one patient who died 4 days after surgery (early fatality) were similar. Because of splenic size the splenic artery could be identified and ligated early in only four patients, two of whom survived and two of whom died >2 months after surgery. In the other 10 patients removal of the spleen required prolonged dissection. Three patients had thickening of the splenic capsule and one patient who died after hospital discharge also had adhesions to other organs. No splenic infarctions were found. One survivor and the patient who died 4 days post-operatively had multilobular spleens. Hepatic cirrhosis was noted in two survivors. Four survivors and two late fatalities had ascites. The largest amount of ascites found was 12.4 liters (late fatality). The spleen was weighed in three patients with Hackett grade 3, 4, and 5 spleens and the weights were 1500, 2160, and 5000 grams, respectively.

Surgery was straightforward and uncomplicated in 10 patients. In one survivor the situation of the pancreatic tail in the splenic hilum required resection of the pancreatic tail, which was covered with an abdominal muscle transplant. In one survivor the situation of the stomach in the splenic hilum required prolonged dissection. There were multiple adhesions between the spleen, colon, stomach, and abdominal wall in one late fatality and a bleeding disorder in the one patient who died in the post-operative period.

Table 1. Pre-operative clinical findings among 14 patients who had elective splenectomy †

Pre-operative clinical findings	*Lived* $N=8$	*Died* $N=6$
Age (years)*	27.3 ± 7.8 (18-40)	26.2 ± 4.2 (20-30)
Sex (M/F)	6/2	6/0
General condition:		
Good	1	0
Fair	3	1
Poor	4	5
Ascites present	4	2
Hackett spleen grade*	4.0 ± 0.9 (3-5)	4.3 ± 1.2 (2-5)
Hemoglobin (gm/dl)*	8.6 ± 2.7 (6.0-12.0)	9.8 ± 1.2 (7.5-11.0)

† No significant difference between groups

* Mean ± SD (range)

Post-operative, in-hospital complications were noted in three survivors, the one early fatality, and in four of the late fatalities. Five patients developed malaria, one survivor had a ruptured wound thought to be secondary to ascites, and one late fatality developed a hernia through the wound site. One patient had persistent bleeding from wound and venipuncture sites, developed hypovolemic shock, and died in the hospital 4 days after the operation.

Patients stayed in the hospital for 25.1 ± 13.2 (mean $\pm$SD) days post-operatively. The five patients who died outside of the hospital were in good condition at the time of discharge.

Follow-up. One patient died in the hospital and five died outside of the hospital. The eight surviving patients were all interviewed in June 1984. The findings in these eight are outlined in *table 2*. The cause and time of death were not established in one patient. Three of the five who died out of hospital probably died because of an infection. The reports from family members regarding the six patients who died are outlined in *table 3*.

Table 2. Condition of the survivors in June 1984

Patient	*Months since operation*	*Condition compared to pre-op**	*Capacity for work**	*Condition assessed by physician or nurse*
1	73	Much better	100%	NR†
2	71	Much better	100%	Normal
3	52	Much better	50%	NR†
4	43	Better	100%	Normal
5	42	Much better	25%	Normal
6	38	Much better	NR†	NR†
7	30	Much better	100%	NR†
8	28	Better	100%	Normal

* Patient's assessment

† NR - not recorded by the physician or nurse who saw the patient

Table 3. Time from operation until death, and clinical diagnosis at time of death in the 6 patients who died

Patient	*Months from splenectomy until death*	*Clinical diagnosis at time of death**
M1	< 20	unknown
M2	20	malaria, pneumonia
M3	11	cerebral malaria
M4	4 days	coagulation defect, hypovolemic shock
M5	11	ascites
M6	2	bronchitis, diarrhea

* As reported by physicians and nurses who responded to the questionnaire (see Methods).

Description of patients excluded from the analysis. A 27-year-old male (E1) in poor condition, with Hackett grade 2 splenomegaly and considerable ascites, was found to have severe, nodular cirrhosis of the liver at the time of surgery and splenectomy was not performed. He was discharged in good condition, but died within 6 weeks of the operation. The cause of death was unknown.

A 13-year-old male (E2) in poor condition, with Hackett grade 2 spleen, massive ascites and a pre-operative diagnosis of cirrhosis and portal hypertension was taken to surgery for a spleno-renal shunt. The spleen was removed, but the shunt could not be performed for technical reasons. He was discharged in good condition and died 2 months post-operatively with the diagnosis of amebic dysentery. The patient had a severely cirrhotic liver.

Discussion

This retrospective analysis was undertaken to determine the long-term mortality of patients who met the indications for surgery (see Methods) and had splenectomy, and to determine whether any patients actually benefited from surgery.

Six of the 14 patients (43%) died from 4 days to 20 months after surgery. The patient with the bleeding disorder who died 4 days post-operatively in hypovolemic shock must be considered an operative fatality. It is uncertain whether the five patients who died from 2 to 20 months after surgery died because the splenectomy made them more susceptible to malaria and other infections, because of their poor general conditions, or because of disease processes unrelated to the splenomegaly or the splenectomy.

The benefits of splenectomy to survivors were quite clear (*table 2*). At least six of the eight had received repeated courses of antimalarials or weekly chemoprophylaxis in the year prior to surgery, but none were able to work pre-operatively. In rural Irianese society, there is little place for an individual who cannot walk through the jungle and mountains and work. All eight patients are now able to work and all eight consider their conditions to be better than prior to the operation (*table 2*). In July 1984, at least five of the eight survivors were working at full capacity. The one patient who was still weak and only able to work at 25% of capacity felt that he was much better than he had been pre-operatively. Despite our advice, only one of the eight patients had been taking regular malaria chemoprophylaxis from the time of splenectomy.

Since we did not have control groups of patients, who were untreated or treated with well-documented malaria chemoprophylaxis, we cannot determine the true risk or benefit of splenectomy in these patients. However, we would like to stress that the patients operated on were a unique group selected for their poor conditions compared with other villagers with splenomegaly. Most splenectomies were undertaken only after repeated requests by referring nurses and physicians and the patients themselves. Despite warnings regarding operative and post-operative mortality, the health workers and patients insisted that the patients' conditions and short-term prognoses were so poor that a substantial risk was worth taking. In both neighboring New Guinea and in Nigeria mortality in patients with untreated TSS [8] or in those who discontinued effective chemoprophylaxis [10] was high. We think, but certainly cannot prove, that some, if not all of the patients who died, as well as some who are still alive, would have already died if they had not been operated on.

Since serum IgM levels were not measured and pathologic examination of the spleen, bone marrow, and liver were not performed, we cannot be certain of the diagnosis of TSS (HMS) in any of the patients [1, 5]. However, the 14 patients were similar in regard to genetic background, living conditions, malaria exposure, and

clinical presentation to patients in neighboring Papua New Guinea with well-documented TSS (HMS) [11, 12]. In Irian Jaya there are no other known infectious causes of massive splenomegaly. Although we cannot exclude non-infectious aetiologies for massive splenomegaly, we think that all 14 patients had tropical splenomegaly syndrome and that the two patients who were excluded from the analysis (E1 and E2) did not have TSS (HMS), but had severe liver disease with moderate splenomegaly.

In summary, we have found that 8 out of 14 patients with massive splenomegaly, thought to be due to TSS (HMS), who underwent splenectomy because they were no longer able to work, are alive and working productively 2 to 6 years later. The true value or risk of splenectomy for massive tropical splenomegaly can only be established by a prospective, randomized study comparing splenectomy and chemoprophylaxis in patients with well-established diagnoses. In the meantime we think that splenectomy is indicated for patients with the clinical diagnosis of TSS who have failed on chemoprophylaxis and whose lives are severely compromised by splenic pain, abdominal mass, or debilitation.

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Between 1978 and 1982, 14 patients underwent splenectomy for disabling, massive splenomegaly at the Regency Hosp. in Wamena in the highlands of Irian Jaya, Indonesia. All patients were clinically diagnosed as having tropical splenomegaly syndrome (hyperreactive malarial splenomegaly), but in no case was the diagnosis confirmed. In May 1984 nurses and physicians caring for these 14 patients were asked to fill in a questionnaire regarding the patients' conditions. Two to 6 years after splenectomy, 8 of the 14 patients were alive and able to work; at least 6 of the 8 at normal or near normal capacity. One patient died 4 days after surgery and 5 died from 2 to 20 months after surgery. We conclude that splenectomy is beneficial for some highly selected patients with the clinical diagnosis of tropical splenomegaly syndrome.

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